

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
19 September 2002 (19.09.2002)

PCT

(10) International Publication Number
WO 02/073507 A2

(51) International Patent Classification⁷: **G06K**
(21) International Application Number: PCT/IL02/00210
(22) International Filing Date: 14 March 2002 (14.03.2002)
(25) Filing Language: English
(26) Publication Language: English
(30) Priority Data:
60/275,486 14 March 2001 (14.03.2001) US
(71) Applicant (for all designated States except US): **GIVEN IMAGING LTD.** [IL/IL]; 2 HaCarmel St., Industrial Park, 20692 Yoqneam (IL).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

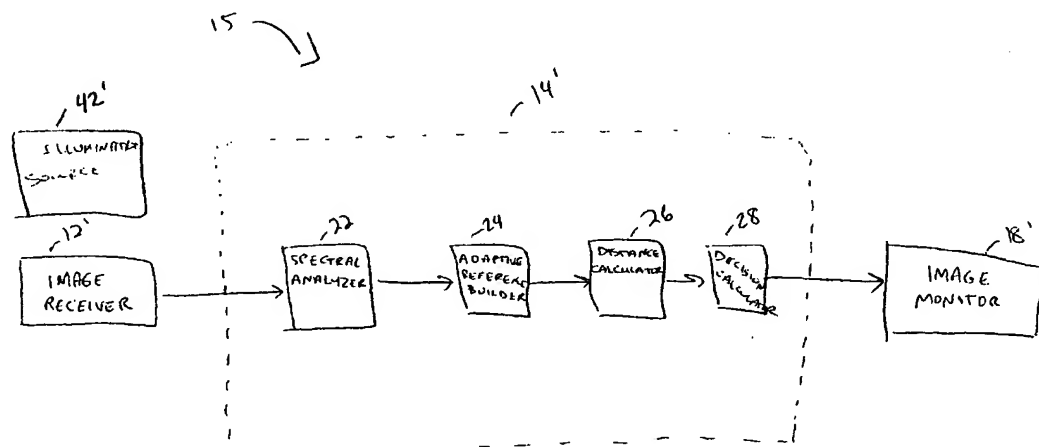
Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(72) Inventors; and
(75) Inventors/Applicants (for US only): **ADLER, Doron** [IL/IL]; 24/5 Hanuriot Street, 36790 Nesher (IL). **ZINATI, Ofra** [IL/IL]; 2/3 David Asaf Street, 34760 Haifa (IL). **LEVY, Daphna** [IL/IL]; 103 Hadas Street, 21661 Carmiel (IL). **GLUKHOVSKY, Arkady** [IL/IL]; 24/5 Hanuriot Street, 36790 Nesher (IL).
(74) Agent: **EITAN, PEARL, LATZER & CO-HEN-ZEDEK**; 2 Gav Yam Center, 7 Shenkar Street, 46725 Herzlia (IL).

(54) Title: METHOD AND SYSTEM FOR DETECTING COLORIMETRIC ABNORMALITIES



(57) Abstract: A system and method for detection of colorimetric abnormalities within a body lumen includes an image receiver for receiving images from within the body lumen. Also included are a transmitter for transmitting the images to a receiver, and a processor for generating a probability indication of presence of colorimetric abnormalities on comparison of color content of the images and at least one reference value.

WO 02/073507 A2

METHOD AND SYSTEM FOR DETECTING COLORIMETRIC ABNORMALITIES IN VIVO

FIELD OF THE INVENTION

5

The present invention relates to a method and system for detection of colorimetric abnormalities in vivo, and specifically within the gastrointestinal (GI) tract.

BACKGROUND OF THE INVENTION

10

Pathologies of the gastrointestinal (GI) tract may exist for a variety of reasons. Some examples of pathologies include bleeding, lesions, angiodysplasia, Crohn's disease, polyps, celiac disorders, and others. The majority of pathologies result in changes of color and/or texture of the inner surface of the GI tract.

15

As one example, color changes may be due to bleeding. Blood may be present within the digestive tract for a variety of pathological reasons, including ulcers, cancer, or other disease conditions. It is often difficult to detect the presence of blood within the GI tract, since bleeding can occur in difficult to reach locations. In addition, it is difficult to "see" inside the tract, especially in sections which are hard to reach such as the small intestines.

20

Several approaches have been used to try to detect the presence of blood within the GI tract. One approach has been the detection of blood in the feces by visual and/or chemical means. The main drawback of this approach has been that the concentration of blood in the feces is lower than the concentration of blood at the bleeding site, since additional materials are accumulated along the GI passage. Therefore, the sensitivity of this approach is low. In addition, the specific bleeding site along the GI tract cannot be determined.

25

A second, more invasive technique, has been the use of an endoscope or enteroscope. This approach enables direct visualization of parts of the GI tract. However, most portions of the small intestine are inaccessible by this method.

30

Other examples of pathologies which may be detected based on the red part of the spectrum include active bleeding, blood clots, polyps, lesions, ulcerations, angiodysplasia and telangiectasia. Pathologies which may be characterized by

blue/violet color include arterio-venous malformation (AVM) and submucosal bleeding. AVM may also appear in red. In addition, some types of ulcers are characterized by white color.

SUMMARY OF THE INVENTION

There is provided, in accordance with one embodiment of the present invention, a method for detecting colorimetric abnormalities in a body lumen. The method includes the step of calculating a probability indication of a presence of an abnormal color within the body lumen based on comparison of spectral characteristics to at least one reference value.

There is provided, in accordance with another embodiment of the present invention, a method for calculation of a reference value for tissue. The method includes the steps of receiving at least a first image and a second image from within a body lumen, selecting blocks of pixels within the images based on colorimetric parameters, averaging the colorimetric parameters of the selected blocks of pixels of the first and second images, and filtering the colorimetric parameters, thereby obtaining a reference value for tissue.

There is provided, in accordance with another embodiment of the present invention, a swallowable capsule for detecting colorimetric abnormalities in a gastrointestinal tract. The capsule includes an image-receiver for receiving images from the gastrointestinal tract, and a processor for generating a probability indication for presence of colorimetric abnormalities by comparing color content of the images to at least one reference value.

There is provided, in accordance with another embodiment of the present invention, an apparatus for determining colorimetric abnormalities within a body lumen. The apparatus includes an image-receiver for receiving images from a body lumen, a spectral analyzer for determining color content of the images, and a processor for generating a probability indication for presence of an abnormal condition by comparing the color content to at least one reference value.

There is provided, in accordance with another embodiment of the present invention, a system for detection of blood within a body lumen. The system includes a swallowable capsule having an in-vivo imager for obtaining images from within the body lumen, a transmitter for transmitting the images to a receiver, and a processor for generating a probability indication of presence of blood based on comparison of color content of the received images and at least one reference value.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will be understood and appreciated more fully from the following detailed description taken in conjunction with the drawings in which:

5 Fig. 1 is a schematic illustration of a prior art in vivo camera system;

 Fig 2 is a schematic illustration of the classification of samples according to their spectral components;

 Fig. 3 is a block diagram illustration of a system according to one embodiment of the present invention;

10 Fig. 4 is a flow chart illustration of the method used by the system shown in Fig. 3; and

 Fig. 5 is a schematic illustration of adaptive building of a reference tissue sample.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a method and system of detection of pathologies by spectral analysis of images captured by a moving in-vivo video camera system. This analysis is based on detection of colorimetric abnormalities, or deviations from an expected spectrum. The in-vivo video camera system may be included on an endoscope, a swallowable capsule, or any other device which is introduced into the body to view the interior.

US Patent No. 5,604,531, assigned to the common assignee of the present application and incorporated herein by reference, teaches an in vivo camera system, which is carried by a swallowable capsule. The in vivo video camera system captures and transmits images of the GI tract while the capsule passes through the GI lumen. In addition to the camera system, the capsule contains an optical system for imaging an area of interest onto the camera system and a transmitter for transmitting the video output of the camera. The capsule can pass through the entire digestive tract and operate as an autonomous video endoscope. It images even the difficult to reach areas of the small intestine.

Reference is made to Fig. 1, which shows a schematic diagram of the system, described in US Patent 5,604,531. The system comprises a capsule 40 having an imager 46, an illumination source 42, and a transmitter 41. Outside the patient's body are an image receiver 12 (usually an antenna array), a storage unit 19, a data processor 14, an image monitor 18, and a position monitor 16. While Fig.1 shows separate monitors, both an image and its position can be presented on a single monitor.

Imager 46 in capsule 40 is connected to transmitter 41 also located in capsule 40. Transmitter 41 transmits images to image receiver 12, which sends the data to data processor 14 and to storage unit 19. Data processor 14 analyzes the data and is in communication with storage unit 19, transferring frame data to and from storage unit 19. Data processor 14 also provides the analyzed data to image monitor 18 and position monitor 16 where the physician views the data. The image monitor presents an image of the GI lumen and the position monitor presents the position in the GI tract at which the image was taken. Data processor 14 can be configured for real time processing or for post processing to be viewed at a later date.

In addition to revealing pathological conditions of the GI tract, the system can provide information about the location of these pathologies.

In a preferred embodiment of the present invention, received images are analyzed for color content. Based on this analysis, as described hereinbelow, determination as to the presence or absence of a colorimetric abnormality may be made. A colorimetric abnormality may indicate a pathological condition, such as bleeding. Other examples of pathologies which may be detected based on the red part of the spectrum include active bleeding, blood clots, polyps, lesions, ulcerations, angiodysplasia and telangiectasia. Pathologies which may be characterized by blue/violet color include arterio-venous malformation (AVM) and submucosal bleeding. AVM may also appear in red. In addition, some types of ulcers are characterized by white color. It will be apparent that the method and system described hereinbelow may be useful in detecting any colorimetric deviation from the normal color content of a body lumen, whether or not a pathological condition is present.

Reference is now made to Fig. 2, which is a schematic illustration of the classification of samples according to their spectral components. Each test sample T is located within a coordinate system represented by the following variables: hue H, saturation S and value V. Hue H represents a number related to the dominant wavelength of the color stimulus, and varies from 0 to 1 as the color changes from red to yellow to green to cyan to blue to magenta and back to red again. Saturation S corresponds to color purity, and in the case of a pure color is equal to 100%. Value V is a measure of relative intensity of color, representing brightness of red, blue and green (RGB). A distance vector $r(B,T)$ between test sample T and an ideal pathology sample B is calculated. Another distance vector $r(R,T)$ between test sample T and a reference sample of healthy tissue R is calculated. The relationship of distance vector $r(B,T)$ and distance vector $r(R,T)$ is calculated. Each test sample T is classified based on the relationship between distance vector $r(B,T)$ and distance vector $r(R,T)$. Briefly, if distance vector $r(B,T)$ is small relative to distance vector $r(R,T)$, there is a positive indication of pathological color. In the preferred embodiment, the analysis is set up to include a higher possibility of false positives than false negatives, so as to minimize the likelihood of missing a positive diagnosis. However, other embodiments of analysis are possible as well.

Reference is now made to Figs. 3 and 4, which illustrate a system 15 and a flow chart diagram showing the steps of using system 15 for determining the blood content or any other color-distinguishable pathology within the gut. System 15 comprises illumination source 42', image receiver 12', data processor 14', and image monitor 18'. Data processor 14' comprises a spectral analyzer 22, an adaptive reference builder 24, a distance calculator 26, and a decision calculator 28. According to one embodiment of the invention, data processor 14' is a standard computer accelerator board, high performance computer, multiprocessor or any other serial or parallel high performance processing machine. Image monitor 18' may be a video display, or a graph, table or any other indicator.

Steps of Fig. 4 may be accomplished using system 15 of Fig. 3. In one embodiment, images are captured and processed within a capsule. In another embodiment, images are captured by an in-vivo system, and are transmitted to a remote location where they are processed. Image receiver 12' receives (step 101) images captured by the in-vivo camera system of Fig. 1 or any other in-vivo imager. Data processor 14' divides (step 102) the color images into a grid of pixels. As in other imaging applications, the number of pixels determines the resolution of the image. For purposes of this discussion, the images are divided into blocks (i,j) of 8 x 8 pixels. Since, in one embodiment, the original image is a 256 x 256 pixel image, the result of dividing into 8 pixels, and determining the color components is a 32 x 32 x 3 matrix of color component value blocks. Spectral analyzer 22 calculates (step 104) the color components of each block: hue H_{ij} ; saturation S_{ij} ; and brightness value V_{ij} for each image.

Spectral analyzer also calculates (steps 105 and 106-110) the color components of blocks of pathology sample B and of healthy reference tissue R. Spectral analyzer 22 calculates (step 105) the color components of blocks of pathology sample B from known images containing blood.

Reference is now made to Fig. 5, which is a schematic illustration of the adaptive reference building steps 106-110 of Fig. 4. Adaptive reference builder 24 calculates (steps 106-110) tissue reference color components in order to build a reference sample of healthy tissue. The adaptive approach is based on averaging healthy tissue appearing in subsequent images. Averages are used since the parameters of healthy tissue along the GI tract may change. Adaptive reference

builder 24 selects (step 107) blocks based on value V (brightness) and hue H. In one embodiment, the conditions are: $0.1 < V_{i,j} < 0.9$ and $0 < H_{i,j} < 0.09$. These conditions indicate that healthy tissue is present. As shown in Fig. 5, images P_i , P_{i-1} , and P_{i-2} with regions R_i , R_{i-1} , and R_{i-2} of healthy tissue are obtained. Adaptive reference
 5 builder 24 averages (step 108) color components of healthy regions R_i , R_{i-1} , and R_{i-2} (i.e. the selected blocks) of images P_i , P_{i-1} , and P_{i-2} obtained along the GI tract. To smooth the data and eliminate sensitivity to particular images, adaptive reference builder 24 filters (step 110) the average tissue colors of the present image P_i and the previous image P_{i-1} .

10 In one embodiment an Infinite Impulse Response (IIR) filter with the following iterative computation is used:

$$out(t_i) = 0.08 * in(t_i) + 0.92 * out(t_{i-1})$$

15 where t_i represents the time index of the current frame i and t_{i-1} represents the time index of the previous frame $i-1$.

Referring back to Fig. 4, distance calculator 26 then calculates (step 112) the Euclidian distance between each block in the matrix and blood reference value B. Blood reference value B is obtained from known images containing blood, analyzed
 20 by spectral analyzer 22 as described above. In another embodiment, a different colorimetric reference value may be used for indication of other unusual colors. The result of this calculation, for the exemplary embodiment, is a matrix of 32×32 elements $\beta_{i,j}$. This calculation is done according to the following equation:

$$\beta_{i,j} = \frac{\sqrt{(H_{i,j} - H_b)^2 + (S_{i,j} - S_b)^2 + (V_{i,j} - V_b)^2}}{\sqrt{(H_b^2 + S_b^2 + V_b^2)} * \sqrt{(H_{i,j}^2 + S_{i,j}^2 + V_{i,j}^2)}}$$

25

where H_b , S_b and V_b are the reference values for hue, saturation and brightness, respectively of blood.

A similar distance calculation is calculated relative to the adaptive tissue reference color (healthy tissue) components, resulting in a 32×32 matrix $\theta_{i,j}$ as
 30 follows.

$$g_{i,j} = \frac{\sqrt{(H_{i,j} - H_t)^2 + (S_{i,j} - S_t)^2 + (V_{i,j} - V_t)^2}}{\sqrt{(H_t^2 + S_t^2 + V_t^2)} * \sqrt{(H_{i,j}^2 + S_{i,j}^2 + V_{i,j}^2)}}$$

where H_t , S_t and V_t are the reference values for hue saturation and brightness, respectively, of healthy tissue.

- 5 Once the distance matrices are obtained, decision calculator 28 calculates (step 116) a probability indication function Λ according to the following equation:

$$\Lambda = \sum_{i,j} \left\{ (\beta_{i,j} \leq \text{BloodThreshold}) \cap \left(\frac{g_{i,j}}{\beta_{i,j}} \geq \text{TissueRatioThreshold} \right) \right\}$$

- The threshold can be set to any value. In a preferred embodiment, the threshold values are as follows: BloodThreshold=0.15 and TissueRatioThreshold=4. Blood
10 exists if $\Lambda > 0$.

Finally, image monitor 18' displays (step 118) the results, either as a color video showing the presence of blood, or as a graph or table indicating the levels and/or threshold values.

- 15 Display of results may include incorporation of a position indicator, so that the end user can determine where the presence of color change is within the GI tract, or other body lumen. Thus, the physician will be able to deal with the problem area.

It will be appreciated by persons skilled in the art that the present invention is not limited to what has been particularly shown and described hereinabove. Rather the scope of the present invention is defined only by the claims that follow:

What is claimed is:

1. A method for detecting abnormalities in-vivo, the method comprising the steps of:
5 analyzing an image for at least one spectral characteristic; and
 creating an abnormality determination based on the analysis.
2. The method of claim 1, wherein the abnormality determination is a determination of the presence of an abnormality.
- 10 3. The method of claim 1, wherein the abnormality determination is a probability determination of the presence of an abnormality.
4. The method of claim 1, wherein analyzing the image includes at least analyzing
15 the image for at least one spectral characteristic in relation to a reference value.
5. The method of claim 1, wherein the image is of a body lumen.
6. A method as in claim 1, wherein said spectral characteristics include hue
20 values.
7. A method as in claim 1, wherein said at least one reference value includes a pathology sample.
- 25 8. A method as in claim 7, wherein said pathology sample includes blood.
9. A method as in claim 1, wherein said abnormality is due to the presence of blood.
- 30 10. A method as in claim 1, wherein said analysis includes comparing images.
11. A method as in claim 1 wherein the image is received from an in-vivo camera imager.

12. A method as in claim 1 wherein the image is received from a capsule.
13. A method according to claim 1, further comprising determining the position of
5 the image.
14. A system for detecting abnormalities in-vivo, the system comprising:
an image receiver means for receiving images;
an analysis means for analyzing an image for at least one spectral
10 characteristic and for making an abnormality determination based on the analysis.
15. A system for detecting abnormalities in-vivo, the system comprising:
an image receiver module capable of receiving images;
an analysis module capable of analyzing an image for at least one spectral
15 characteristic and making an abnormality determination based on the analysis.
16. The system of claim 15 wherein the abnormality determination is a probability.
17. The system of claim 15, wherein analyzing the image includes at least
20 analyzing the image for at least one spectral characteristic in relation to a
reference value.
18. The system of claim 15, wherein the image is of a body lumen.
- 25 19. The system as in claim 17, wherein said at least one reference value includes a
healthy tissue reference value.
20. The system as in claim 17, wherein said at least one reference value includes a
pathology sample.
- 30 21. The system as in claim 20, wherein said pathology sample includes blood.

22. The system as in claim 15, wherein said abnormality is due to the presence of blood.
23. The system as in claim 15, wherein said analysis includes comparing images.
- 5 24. The system as in claim 15 wherein the image is received from an in-vivo camera imager.
25. The system as in claim 15 wherein the image is received from a capsule.
- 10 26. A method for calculation of a reference value for tissue, the method comprising the steps of:
- receiving at least a first image and a second image from within a body lumen;
 - selecting blocks of pixels within said images based on colorimetric
 - 15 parameters;
 - averaging said colorimetric parameters of said selected blocks of pixels of said at least first and second images; and
 - filtering said colorimetric parameters, thereby obtaining a reference value for tissue.
- 20 27. A method as in claim 26, wherein said step of receiving includes receiving multiple images.
28. A method as in claim 26, wherein said colorimetric parameters include hue.
29. A method as in claim 26, wherein said colorimetric parameters include brightness.
- 25 30. A method as in claim 26, wherein said tissue is healthy tissue.
31. A swallowable capsule for detecting colorimetric abnormalities in a gastrointestinal tract, the capsule comprising:
- an image-receiver for receiving images from said gastrointestinal tract; and
 - a processor for generating a probability indication for presence of
 - 30 colorimetric abnormalities by comparing color content of said images to at least one reference value.
32. A capsule as in claim 31, wherein said at least one reference value is a pathology sample.

33. A capsule as in claim 32 wherein said pathology sample includes blood.
34. A capsule as in claim 31, wherein said at least one reference value includes a healthy tissue reference sample.
35. A capsule as in claim 31, wherein said at least one reference value includes a pathology sample.
36. A capsule as in claim 31, wherein said color content includes spectral characteristics.
37. A capsule as in claim 36, wherein said spectral characteristics include hue.
38. A capsule as in claim 36, wherein said spectral characteristics include saturation.
39. A capsule as in claim 36 wherein said spectral characteristics include brightness.
40. An apparatus for determining colorimetric abnormalities within a body lumen, said apparatus comprising:
- an image-receiver capable of receiving images from a body lumen;
- a spectral analyzer capable of determining color content of said images;
- and
- a processor capable of generating a probability indication for presence of an abnormal condition by comparing said color content to at least one reference value.
41. An apparatus as in claim 40 wherein said processor is configured for real-time processing.
42. An apparatus as in claim 40, wherein said processor is configured for post-processing.
43. An apparatus as in claim 40, wherein said pathological condition includes bleeding
44. An apparatus as in claim 40, wherein said at least one reference value includes a value for healthy tissue.
45. An apparatus as in claim 40, wherein said at least one reference value includes a value for pathological tissue.
46. A system for detection of a colorimetric abnormality within the gastrointestinal tract, said system comprising:
- a swallowable capsule having an in-vivo imager for obtaining images from within said body lumen;

a transmitter capable of transmitting said images to a receiver; and
a processor capable of generating a probability indication of presence of
blood based on comparison of color content of said received images and at
least one reference value.

5 47. A system according to claim 36 wherein said colorimetric abnormality indicates
a pathological condition.

48. A system according to claim 37 wherein said pathological condition includes
bleeding.

49. A system according to claim 36 wherein said at least one reference value
10 includes a value for healthy tissue.

50. A system according to claim 36 wherein said at least one reference value
includes a value for pathological tissue.

51. A system according to claim 36, further comprising a position indicator, thereby
allowing visualization of a location of said results within said body lumen.

15 52. A method for detecting abnormalities in-vivo, the method comprising the steps
of:

analyzing an image stream for at least one spectral characteristic;
creating an abnormality determination based on the analysis; and
20 presenting to a user the abnormality determination.

53. The method of claim 52, wherein the abnormality determination is a
determination of the probability of an abnormality.

25 54. The method according to claim 1, wherein the image is part of an image
stream.

55. An apparatus for determining colorimetric abnormalities in-vivo, said apparatus
comprising:

30 an image-receiver capable of receiving images; and
a processor capable of analyzing color content of said images, generating a
an abnormality indication for the presence of an abnormal condition and presenting
to a user an abnormality diagnosis.

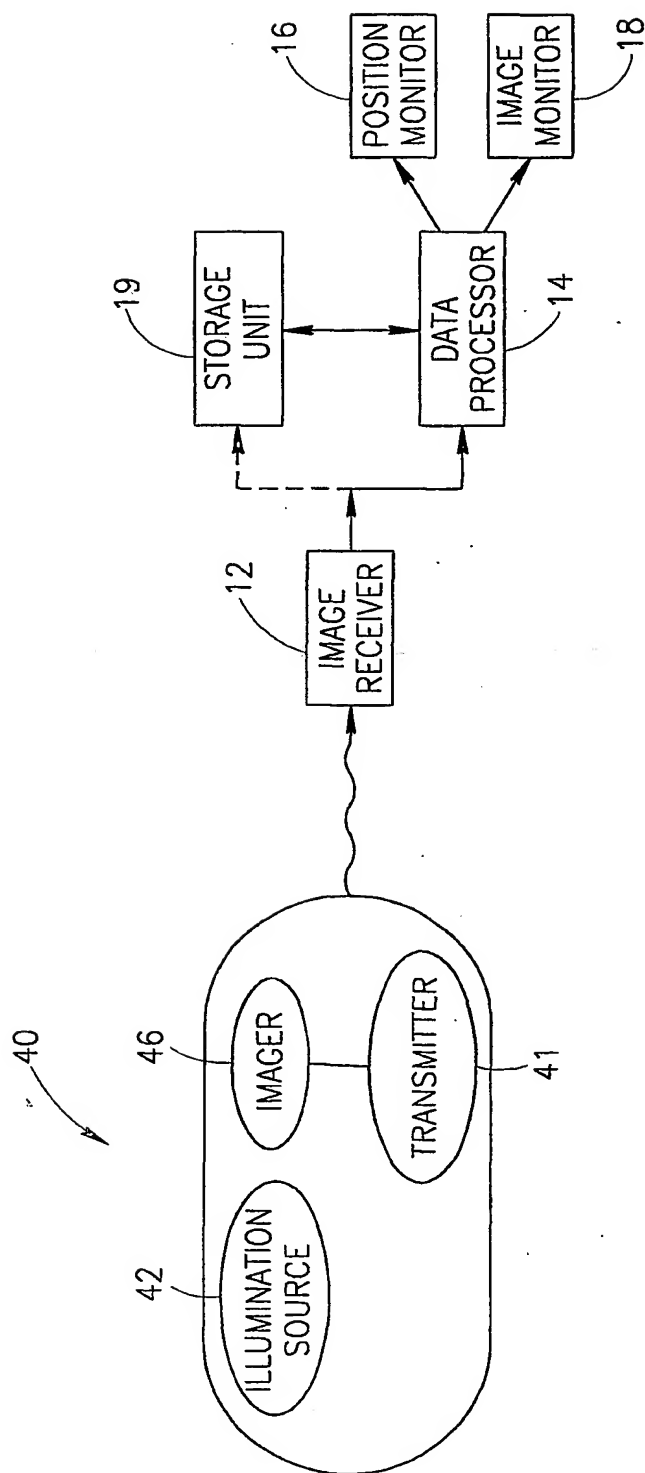
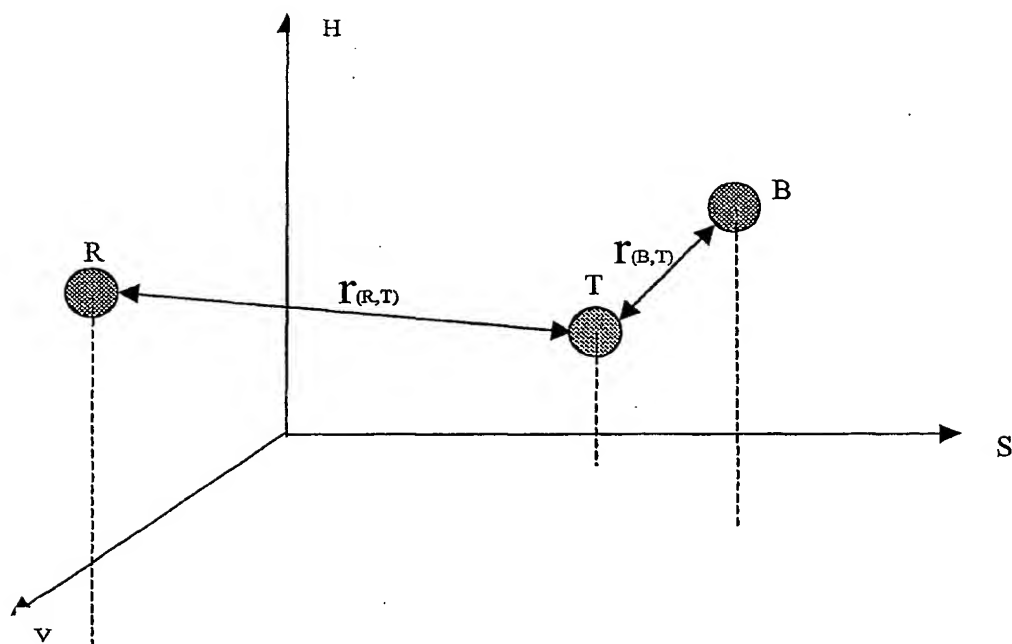


FIG.1
PRIOR ART

Figure 2

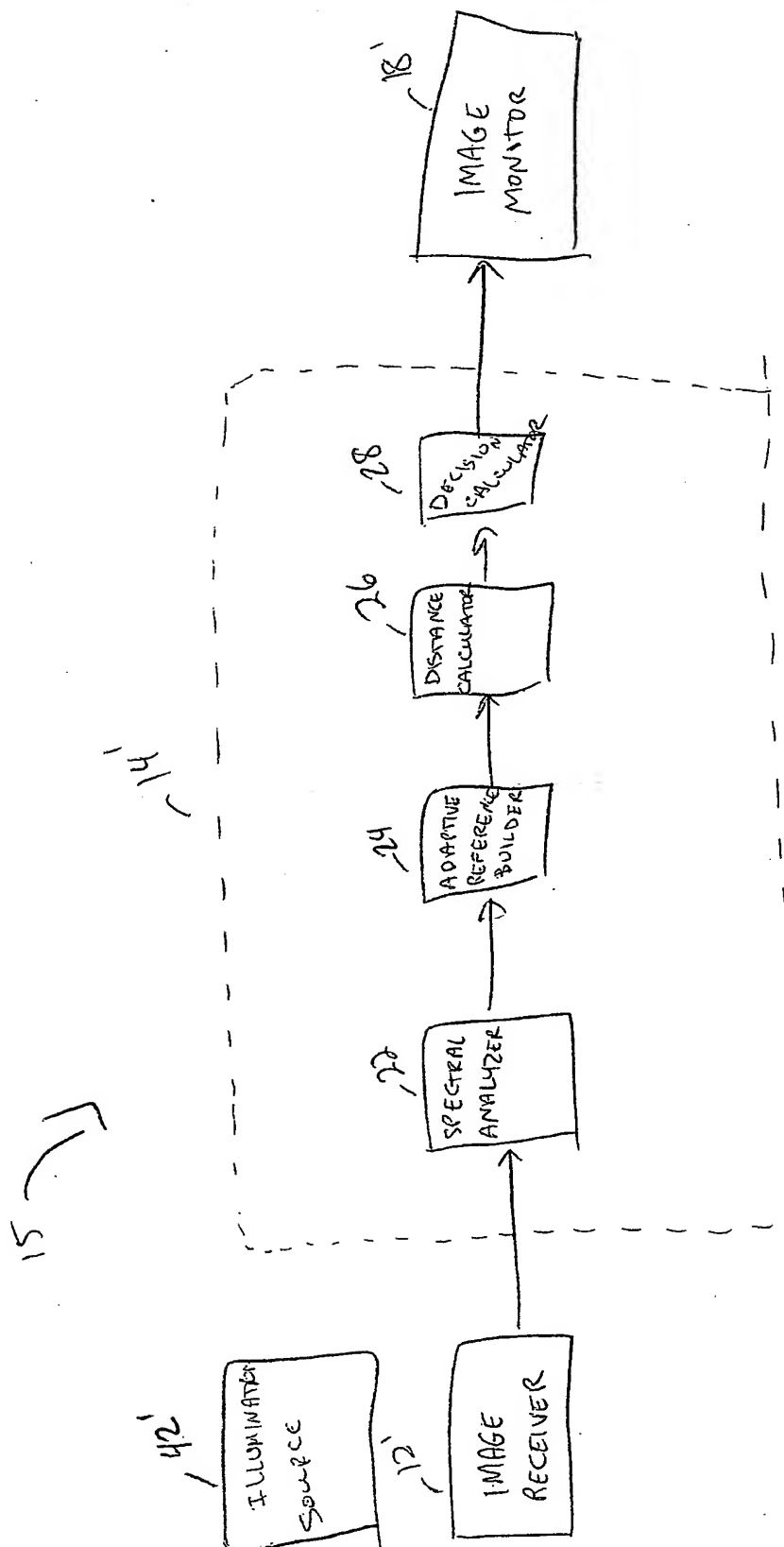
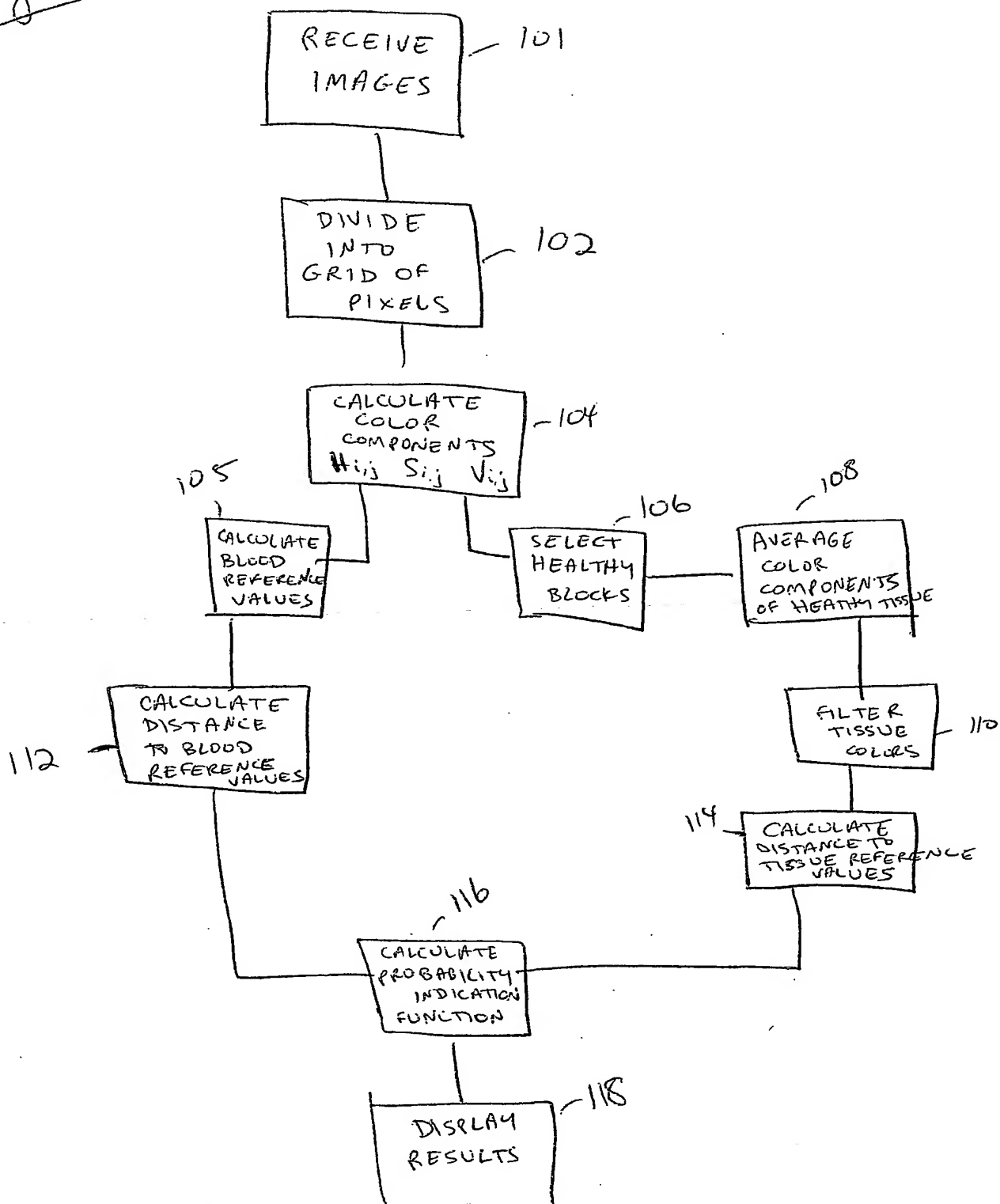
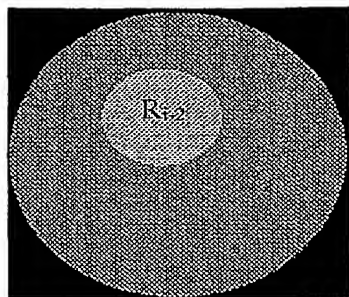
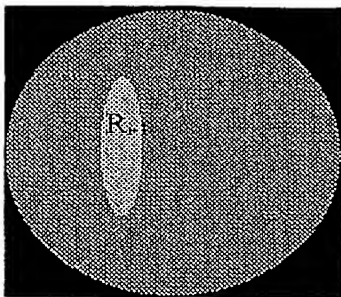


Fig. 3

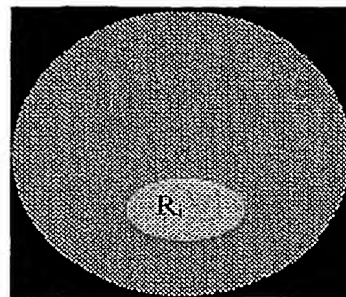
Fig. 4



P_{i-2}



P_{i-1}



P_i

Figure 5

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☒ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☐ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.